

Claims:

1. A method for the highly sensitive simultaneous measurement of nonlinear optical emission signals, spatially resolved in one or two spatial dimensions, comprising:
 - radiating the excitation light from at least one light source in a power-modulated and/or pulse-duration-modulated form into an interaction volume or to an interaction area or an interaction layer (referred to jointly by the designation "interaction spaces"), in each of which interaction spaces one or a plurality of emissions that are correlated nonlinearly with the excitation light can be excited,
 - measuring the light emerging from said interaction spaces by means of a one- or two-dimensional detector array,
 - transmitting the measurement data from said detector array to a computer and formatting the data in a one- or multidimensional data matrix, characterized in that those portions of the light emerging from the interaction spaces which are linearly proportional to the intensity of the excitation light available in the interaction spaces are separated from portions of the light emerging from the interaction spaces which are nonlinearly proportional to the available excitation light intensity.
2. The method as claimed in claim 1, characterized in that it does not comprise any spectral filtering of the light that is to be detected and emerges from the interaction spaces.
3. The method as claimed in claim 1, characterized in that it is carried out in combination with a spectral filtering of the light that is to be detected and emerges from the interaction spaces.
4. The method as claimed in one of claims 1 - 3, characterized in that said one- or two-dimensional detector array is selected from the group comprising CCD cameras, CCD chips, CMOS cameras, CMOS chips, photodiode arrays, avalanche diode arrays, multichannel plates and multichannel photomultipliers, it being possible for a phase-sensitive demodulation to be integrated into said

detector array.

5. The method as claimed in one of claims 1 - 4, characterized in that the modulation of the excitation light radiated in to an interaction space is effected by means of optomechanical and/or acousto-optical and/or electro-optically active auxiliary means.
10. The method as claimed in claim 5, characterized in that said optomechanical and/or acousto-optical and/or electro-optically active auxiliary means are selected from the group comprising mechanical shutters and rotating choppers which in each case alternately block and release the light path between the excitation light source and the interaction space, polarization-selective components such as, for example, rotating half-wave plates in combination with polarizers, liquid crystal attenuators, electro-optically active crystals, neutral density filters that are locally or temporally variable in terms of their transmission, acousto-optical modulators and also modulators based on interference effects, such as, for example, Michelson interferometers or Mach-Zehnder interferometers.
20. 7. The method as claimed in one of claims 1 - 4, characterized in that the modulation of the excitation light radiated in to an interaction space is effected by means of direct, active modulation of the light radiated from the excitation light source.
25. 8. The method as claimed in claim 7, characterized in that the modulation of the excitation light radiated in to an interaction space is effected by means of modulation of the excitation current for a semiconductor laser as excitation light source.
30. 9. The method as claimed in one of claims 1 - 8, characterized in that the modulation of the excitation light radiated in to an interaction space is effected periodically.
10. The method as claimed in one of claims 1 - 8, characterized in that the

modulation of the excitation light radiated in to an interaction space is effected non-periodically.

11. The method as claimed in one of claims 1 - 10, characterized in that the 5 modulation of the excitation light radiated in to an interaction space consists in the modulation of the intensity radiated in.

12. The method as claimed in one of claims 1 - 10, characterized in that the 10 modulation of the excitation light radiated in to an interaction space consists in the simultaneous modulation of the pulse duration and the peak power of the excitation light radiated in, the peak power preferably being varied inversely proportionally to the pulse duration and the integral of the pulse power particularly preferably remaining constant.

15 13. The method as claimed in one of claims 1 - 12, characterized in that it is effected without detection of the modulated excitation light or a measurement variable proportional thereto.

14. The method as claimed in one of claims 1 - 12, characterized in that it 20 comprises, in addition to the detection of the light emerging from the interaction spaces, the detection of the modulated excitation light or a measurement variable proportional thereto.

15. The method as claimed in one of claims 1 - 14, characterized in that the 25 detection of the light emerging from the interaction spaces is effected in a manner temporally correlated with the modulation of the excitation light power.

16. The method as claimed in claim 15, characterized in that the detection of the light emerging from the interaction spaces is effected with a frequency 30 corresponding to an integer multiple of the modulation frequency of the excitation light power.

17. The method as claimed in one of claims 1 - 16, characterized in that the separation of the response signal portions from the interaction space that are

correlated nonlinearly with the excitation light power from the remaining signal portions is effected with the aid of a parallel series expansion.

18. The method as claimed in one of claims 1 - 17, characterized in that the
5 separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected with the aid of a parallel Taylor expansion.

19. The method as claimed in one of claims 1 - 16, characterized in that the
10 separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected with the aid of a harmonic analysis.

20. The method as claimed in one of claims 1 - 16, characterized in that the
15 separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected by means of a stepped modulation of the excitation light power.

20 21. The method as claimed in one of claims 1 - 16, characterized in that the
separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected using a four-step algorithm for the modulation of the excitation light power.

25 22. The method as claimed in one of claims 1 - 21, characterized in that experimentally dictated deviations of the excitation light powers from the desired values provided for the modulation are compensated for by means of numerical corrections.

30 23. The method as claimed in one of claims 21 - 22, characterized in that the response signals measured using a four-step algorithm for the modulation are multiplied by correction factors.

24. The method as claimed in claim 23, characterized in that the correction factors for the response signals are determined from measured excitation light powers for the generation of said response signals.

5 25. The method as claimed in claim 23, characterized in that the correction factors for the response signals are determined by a numerical analysis of the response signal data generated, it being possible for this to be effected for example by evaluation of the signals from partial regions – identified for this – of an interaction space or with the aid of separate measurements (for example using a 10 calibration sample).

15 26. The method as claimed in one of claims 1 - 25, characterized in that the separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected in real time contemporaneously (within the recording time for the signal recording) with the recording of the signals from the interaction space.

20 27. The method as claimed in one of claims 1 - 26, characterized in that the interaction space is an interaction layer at a surface of a fixed carrier, the areal extent of the interaction space (on said surface of this carrier) being defined by the interaction area with the impinging power-modulated excitation light and its depth (extent perpendicular to said surface of the carrier) being defined by the range of the modulated excitation light intensity in this space dimension perpendicular to said surface of the carrier.

25 28. The method as claimed in claim 27, characterized in that there are situated within the interaction space compounds or substances or molecular subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the 30 interaction thereof with further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated.

29. The method as claimed in claim 27, characterized in that there are immobilized on the surface of said fixed carrier one or a plurality of specific

binding partners for the detection of one or a plurality of analytes in a binding assay (with the binding partner from a supplied solution binding to the immobilized binding partner), the analyte detection being effected on the basis of an optical response signal – correlated nonlinearly with the excitation light power – of the immobilized binding partner itself or of the binding partner supplied in solution or of one or a plurality of further binding partners supplied in one or a plurality of additional method steps.

5 30. The method as claimed in claim 29, characterized in that the specific binding partners immobilized on the surface of said fixed carrier are the one or the plurality of analytes themselves which are immobilized in a manner embedded in a native sample matrix or in a form of the sample matrix that is modified by means of one or a plurality of conditioning steps.

10 15. 31. The method as claimed in claim 29, characterized in that the specific binding partners immobilized on the surface of said fixed carrier are biological or biochemical or synthetic identification elements for the specific identification of one or a plurality of analytes situated in a supplied sample.

20 25. 32. The method as claimed in one of claims 29 - 31, characterized in that said binding partners, that is to say the analytes to be detected that are themselves immobilized or the analytes to be detected in a supplied sample and/or their biological or biochemical or synthetic identification elements that are immobilized or supplied in a supplied detection reagent, are selected from the group comprising proteins, for example monoclonal, or polyclonal antibodies and antibody fragments, peptides, enzymes, glycopeptides, oligosaccharides, lectins, antigens for antibodies, proteins functionalized with additional binding sites ("tag proteins", such as, for example, "histidine tag proteins"), and also nucleic acids (for example DNA, RNA, oligonucleotides) and nucleic acid analogs (e.g. PNA), aptamers, membrane-bound and isolated receptors and ligands thereof, cavities produced by chemical synthesis for receiving molecular imprints, natural and synthetic polymers, etc.

30 33. The method as claimed in one of claims 28 - 32, characterized in that, on

the surface of said fixed carrier, applied compounds or substances or molecular subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the interaction thereof with further compounds present in the interaction space, optical
5 signals correlated nonlinearly with the excitation light can be generated, or applied specific binding partners are immobilized in discrete measurement regions (spots) which may have an arbitrary geometry, for example circular, oval, triangular, rectangular, polygonal form, etc., it being possible for an individual measurement region to contain identical or different compounds or substances or molecular
10 subgroups or specific binding partners.

34. The method as claimed in claim 33, characterized in that discrete measurement regions are produced by spatially selective application of compounds or substances or molecular subgroups which, under the action of the
15 excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the interaction thereof with further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated, or of specific binding partners on said fixed carrier, preferably using one or a plurality of methods from the group of
20 methods comprising "inkjet spotting", mechanical spotting, "microcontact printing", fluidic contacting of the regions for the measurement regions to be created with the compounds to be immobilized by supplying the latter in parallel or crossed microchannels, under the action of pressure differences or electrical or electromagnetic potentials, and also photochemical and photolithographic
25 immobilization methods.

35. The method as claimed in one of claims 33 - 34, characterized in that there are applied between the spatially separate measurement regions or in unoccupied partial regions within said measurement regions compounds that are "chemically
30 neutral" with respect to the analytes and/or with respect to its binding partners, preferably for example comprising the groups comprising albumins, in particular calf serum albumin or human serum albumin, casein, nonspecific, polyclonal or monoclonal antibodies, heterologous antibodies or antibodies that are empirically nonspecific to the analyte or analytes to be detected and the binding partners

thereof (in particular for immunoassays), detergents – such as, for example, Tween 20 -, fragmented natural or synthetic DNA that does not hybridize with polynucleotides to be analyzed, such as, for example, extracts of herring or salmon sperm (in particular for polynucleotide hybridization assays), or else 5 uncharged but hydrophilic polymers, such as, for example, polyethylene glycols or dextrans.

36. The method as claimed in one of claims 28 - 32, characterized in that, at the surface of said fixed carrier, applied compounds or substances or molecular 10 subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the interaction thereof with further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated, or applied specific binding partners are immobilized directly or by means of a so-called 15 spacer (formed as an independent molecule or molecular group) at the surface of said fixed carrier, with utilization of one or a plurality of types of interactions from the group of interactions comprising hydrophilic interactions, electrostatic interactions and covalent binding.

20 37. The method as claimed in one of claims 28 - 36, characterized in that an adhesion promoting layer is applied between the surface of said fixed carrier and the immobilized compounds or substances or molecular subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the interaction thereof with 25 further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated, or the applied specific binding partners, which adhesion promoting layer preferably has a thickness of less than 200 nm, particularly preferably of less than 20 nm, and preferably comprises a chemical compound from the groups comprising silanes, 30 functionalized silanes, epoxides, functionalized, charged or polar polymers and "self-assembled passive or functionalized monolayers or multilayers", thiols, alkyl phosphates and phosphonates, multifunctional block copolymers, such as, for example, poly(L)lysine/polyethylene glycols.

38. The method as claimed in one of claims 31 - 37, characterized in that more than 10, preferably more than 100, particularly preferably more than 1000 measurement regions are arranged on a square centimeter in a two-dimensional arrangement on the surface of said fixed carrier.

5

39. The method as claimed in one of claims 27 - 38, characterized in that said fixed carrier is optically transparent at the wavelength of the acting excitation light.

10

40. The method as claimed in one of claims 27 - 39, characterized in that said fixed carrier is essentially planar.

15

41. The method as claimed in one of claims 27 - 40, characterized in that said fixed carrier comprises an optical waveguide structure, comprising one or a plurality of layers.

42. The method as claimed in one of claims 27 - 41, characterized in that said fixed carrier comprises a planar optical waveguide that is continuous or divided into discrete wave-guiding regions, comprising one or a plurality of layers.

20

43. The method as claimed in one of claims 27 - 42, characterized in that said fixed carrier comprises a planar optical thin-film waveguide with an essentially optically transparent, wave-guiding layer (a) on a second, likewise essentially optically transparent layer (b) having a lower refractive index than layer (a) and, if appropriate, a likewise essentially optically transparent intermediate layer (b') between layer (a) and layer (b) likewise having a lower refractive index than layer (a).

30

44. The method as claimed in one of claims 41 - 43, characterized in that a wave-guiding layer of said fixed carrier is in optical contact with one or a plurality of optical coupling elements which enable excitation light to be coupled into said wave-guiding layer, said optical coupling elements being selected from the group of prism couplers, evanescent couplers with united optical waveguides with overlapping evanescent fields, end face couplers with focusing lenses, preferably

cylindrical lenses, arranged before an end side of said wave-guiding layer of the evanescent field sensor platform, and grating couplers.

45. The method as claimed in one of claims 41 - 44, characterized in that one 5 or a plurality of grating structures (c) which enable excitation light to be coupled in are fashioned in a wave-guiding layer of the fixed carrier.

46. The method as claimed in one of claims 41 - 45, characterized in that one 10 or a plurality of grating structures (c') having an identical or different grating period and grating depth with respect to grating structures (c) are fashioned in a wave-guiding layer of the fixed carrier and enable light guided in said wave-guiding layer to be coupled out.

47. The method as claimed in one of claims 1 - 46, characterized in that said 15 optical emission signals that are correlated nonlinearly with the excitation light intensity comprise the signals of a frequency doubling ("second harmonic generation"), summation or differential frequency generation.

48. The method as claimed in one of claims 1 - 47, characterized in that said 20 optical emission signals that are correlated nonlinearly with the excitation light intensity are induced by a multi-photon absorption.

49. The method as claimed in claim 48, characterized in that said optical 25 emission signals that are correlated nonlinearly with the excitation light intensity are induced by a two-photon absorption.

50. An analytical system for the highly sensitive simultaneous measurement of nonlinear optical emission signals, spatially resolved in one or two spatial dimensions, comprising:

30

- at least one light source for emitting excitation light,
- technical auxiliary means for the power modulation and/or pulse duration modulation of the excitation light emerging from the at least one light source,
- an interaction volume or an interaction area or an interaction layer,

designated jointly as "interaction space", wherein one or a plurality of emissions that are correlated nonlinearly with the excitation light can be excited,

- at least one one- or two-dimensional detector array for measuring the light emerging from the interaction space,
- a computer to which the measurement data of said detector arrays are transmitted and with the aid of which the measurement data are formatted in a one- or multidimensional data matrix and analyzed,

characterized in that those portions of the light emerging from the interaction spaces which are linearly proportional to the intensity of the excitation light available in the interaction spaces are separated from portions of the light emerging from the interaction spaces which are nonlinearly proportional to the available excitation light intensity.

15 51. The analytical system as claimed in claim 50, characterized in that it does not comprise any components for a spectral filtering of the light that is to be detected and emerges from the interaction spaces.

20 52. The analytical system as claimed in claim 50, characterized in that it additionally comprises components for a spectral filtering of the light that is to be detected and emerges from the interaction spaces.

25 53. The analytical system as claimed in one of claims 50 - 52, characterized in that the at least one one- or two-dimensional detector array is selected from the group comprising CCD cameras, CCD chips, CMOS cameras, CMOS chips, photodiode arrays, avalanche diode arrays, multichannel plates and multichannel photomultipliers, it being possible for a phase-sensitive demodulation to be integrated into said detector array.

30 54. The analytical system as claimed in one of claims 50 - 53, characterized in that said technical auxiliary means for the modulation of the excitation light radiated in to an interaction space are selected from the group comprising optomechanical, acousto-optical and electro-optically active auxiliary means.

55. The analytical system as claimed in claim 54, characterized in that said optomechanical and/or acousto-optical and/or electro-optically active auxiliary means are selected from the group comprising mechanical shutters and rotating choppers which in each case alternately block and release the light path between 5 the excitation light source and the interaction space, polarization-selective components such as, for example, rotating half-wave plates in combination with polarizers, liquid crystal attenuators, electro-optically active crystals, neutral density filters that are locally or temporally variable in terms of their transmission, acousto-optical modulators and also modulators based on interference effects, 10 such as, for example, Michelson interferometers or Mach-Zehnder interferometers.

56. The analytical system as claimed in one of claims 50 - 53, characterized in that the modulation of the excitation light radiated in to an interaction space is 15 effected by means of direct, active modulation of the light radiated from the excitation light source.

57. The analytical system as claimed in claim 56, characterized in that the modulation of the excitation light radiated in to an interaction space is effected by 20 means of modulation of the excitation current for a semiconductor laser as excitation light source.

58. The analytical system as claimed in one of claims 50 - 57, characterized in that the modulation of the excitation light radiated in to an interaction space is 25 effected periodically.

59. The analytical system as claimed in one of claims 50 - 57, characterized in that the modulation of the excitation light radiated in to an interaction space is effected non-periodically.

30 60. The analytical system as claimed in one of claims 50 - 59, characterized in that the modulation of the excitation light radiated in to an interaction space consists in the modulation of the intensity radiated in.

61. The analytical system as claimed in one of claims 50 - 59, characterized in that the modulation of the excitation light radiated in to an interaction space consists in the simultaneous modulation of the pulse duration and the peak power of the excitation light radiated in, the peak power preferably being varied inversely proportionally to the pulse duration and the integral of the pulse power particularly preferably remaining constant.

5

62. The analytical system as claimed in one of claims 50 - 61, characterized in that it is effected without detection of the modulated excitation light or a measurement variable proportional thereto.

10

63. The analytical system as claimed in one of claims 50 - 61, characterized in that it comprises, in addition to the detection of the light emerging from the interaction spaces, a detection of the modulated excitation light or a measurement variable proportional thereto.

15

64. The analytical system as claimed in one of claims 50 - 63, characterized in that the detection of the light emerging from the interaction spaces is effected in a manner temporally correlated with the modulation of the excitation light power.

20

65. The analytical system as claimed in claim 64, characterized in that the detection of the light emerging from the interaction spaces is effected with a frequency corresponding to an integer multiple of the modulation frequency of the excitation light power.

25

66. The analytical system as claimed in one of claims 50 - 65, characterized in that the separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected with the aid of a parallel series expansion, preferably with the aid of a parallel Taylor expansion.

30

67. The analytical system as claimed in one of claims 50 - 65, characterized in that the separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining

signal portions is effected with the aid of a harmonic analysis.

68. The analytical system as claimed in one of claims 50 - 65, characterized in that the separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected by means of a stepped modulation of the excitation light power.

69. The analytical system as claimed in one of claims 50 - 65, characterized in that the separation of the response signal portions from the interaction space that are correlated nonlinearly with the excitation light power from the remaining signal portions is effected using a four-step algorithm for the modulation of the excitation light power.

70. The analytical system as claimed in one of claims 50 - 69, characterized in that the interaction space is an interaction layer at a surface of a fixed carrier, the areal extent of the interaction space (on said surface of this carrier) being defined by the interaction area with the impinging power-modulated excitation light and its depth (extent perpendicular to said surface of the carrier) being defined by the range of the modulated excitation light intensity in this space dimension perpendicular to said surface of the carrier.

71. The analytical system as claimed in claim 70, characterized in that there are situated within the interaction space compounds or substances or molecular subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which, after the interaction thereof with further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated.

72. The analytical system as claimed in claim 70, characterized in that there are immobilized on the surface of said fixed carrier one or a plurality of specific binding partners for the detection of one or a plurality of analytes in a binding assay (with the binding partner from a supplied solution binding to the immobilized binding partner), the analyte detection being effected on the basis of

an optical response signal – correlated nonlinearly with the excitation light power – of the immobilized binding partner itself or of the binding partner supplied in solution or of one or a plurality of further binding partners supplied in one or a plurality of additional method steps.

5

73. The analytical system as claimed in claim 72, characterized in that the specific binding partners immobilized on the surface of said fixed carrier are the one or the plurality of analytes themselves which are immobilized in a manner embedded in a native sample matrix or in a form of the sample matrix that is 10 modified by means of one or a plurality of conditioning steps.

74. The analytical system as claimed in claim 72, characterized in that the specific binding partners immobilized on the surface of said fixed carrier are biological or biochemical or synthetic identification elements for the specific 15 identification of one or a plurality of analytes situated in a supplied sample.

75. The analytical system as claimed in one of claims 72 - 74, characterized in that said binding partners, that is to say the analytes to be detected that are themselves immobilized or the analytes to be detected in a supplied sample and/or 20 their biological or biochemical or synthetic identification elements that are immobilized or supplied in a supplied detection reagent, are selected from the group comprising proteins, for example monoclonal, or polyclonal antibodies and antibody fragments, peptides, enzymes, glycopeptides, oligosaccharides, lectins, antigens for antibodies, proteins functionalized with additional binding sites ("tag 25 proteins", such as, for example, "histidine tag proteins"), and also nucleic acids (for example DNA, RNA, oligonucleotides) and nucleic acid analogs, (eg. PNA), aptamers, membrane-bound and isolated receptors and ligands thereof, cavities produced by chemical synthesis for receiving molecular imprints, natural and synthetic polymers, etc.

30

76. The analytical system as claimed in one of claims 71 - 75, characterized in that, on the surface of said fixed carrier, applied compounds or substances or molecular subgroups which, under the action of the excitation light, are capable of emitting optical signals correlated nonlinearly therewith, or with the aid of which,

after the interaction thereof with further compounds present in the interaction space, optical signals correlated nonlinearly with the excitation light can be generated, or applied specific binding partners are immobilized in discrete measurement regions (spots) which may have an arbitrary geometry, for example

5 circular, oval, triangular, rectangular, polygonal form, etc., it being possible for an individual measurement region to contain identical or different compounds or substances or molecular subgroups or specific binding partners.

77. The analytical system as claimed in claim 76, characterized in that more
10 than 10, preferably more than 100, particularly preferably more than 1000 measurement regions are arranged on a square centimeter in a two-dimensional arrangement on the surface of said fixed carrier.

78. The analytical system as claimed in one of claims 70 - 77, characterized in
15 that said fixed carrier is optically transparent at the wavelength of the acting excitation light.

79. The analytical system as claimed in one of claims 70 - 78, characterized in
that said fixed carrier is essentially planar.

20 80. The analytical system as claimed in one of claims 70 - 79, characterized in
that said fixed carrier comprises an optical waveguide structure, comprising one or a plurality of layers.

25 81. The analytical system as claimed in one of claims 70 - 80, characterized in
that said fixed carrier comprises a planar optical waveguide that is continuous or divided into discrete wave-guiding regions, comprising one or a plurality of layers.

30 82. The analytical system as claimed in one of claims 70 - 81, characterized in
that said fixed carrier comprises a planar optical thin-film waveguide with an essentially optically transparent, wave-guiding layer (a) on a second, likewise essentially optically transparent layer (b) having a lower refractive index than layer (a) and, if appropriate, a likewise essentially optically transparent

intermediate layer (b') between layer (a) and layer (b) likewise having a lower refractive index than layer (a).

83. The analytical system as claimed in one of claims 80 - 82, characterized in
5 that a wave-guiding layer of said fixed carrier is in optical contact with one or a plurality of optical coupling elements which enable excitation light to be coupled into said wave-guiding layer, said optical coupling elements being selected from the group of prism couplers, evanescent couplers with united optical waveguides with overlapping evanescent fields, end face couplers with focusing lenses,
10 preferably cylindrical lenses, arranged before an end side of said wave-guiding layer of the evanescent field sensor platform, and grating couplers.

84. The analytical system as claimed in one of claims 80 - 83, characterized in
15 that one or a plurality of grating structures (c) which enable excitation light to be coupled in are fashioned in a wave-guiding layer of the fixed carrier.

85. The analytical system as claimed in one of claims 80 - 84, characterized in
that one or a plurality of grating structures (c') having an identical or different
20 grating period and grating depth with respect to grating structures (c) are fashioned in a wave-guiding layer of the fixed carrier and enable light guided in said wave-guiding layer to be coupled out.

86. The analytical system as claimed in one of claims 50 - 85, characterized in
25 that said optical emission signals that are correlated nonlinearly with the excitation light intensity comprise the signals of a frequency doubling ("second harmonic generation"), summation or differential frequency generation.

87. The analytical system as claimed in one of claims 50 - 86, characterized in
30 that said optical emission signals that are correlated nonlinearly with the excitation light intensity are induced by a multi-photon absorption.

88. The analytical system as claimed in claim 87, characterized in that said optical emission signals that are correlated nonlinearly with the excitation light intensity are induced by a two-photon absorption.

89. The use of a method as claimed in one of claims 1-49 and/or of an analytical system as claimed in one of claims 50-88 for quantitative and/or qualitative analyses for determining chemical, biochemical or biological analytes

5 in screening methods in pharmaceutical research, combinatorial chemistry, clinical and preclinical development, for real-time binding studies and for determining kinetic parameters in affinity screening and in research, for qualitative and quantitative analyte determinations, in particular for DNA and RNA analysis and the determination of genomic or proteomic differences in the

10 genome, such as, for example, single nucleotide polymorphisms, for measuring protein-DNA interactions, for determining control mechanisms for mRNA expression and for protein (bio)synthesis, for drawing up toxicity studies and also for the determination of expression profiles, in particular for determining biological and chemical marker substances, such as mRNA, proteins, peptides or

15 low molecular weight organic (messenger) substances, but also for detecting antibodies, antigens, pathogens or bacteria in pharmaceutical product research and development, human and veterinary diagnosis, agrochemical product research and development, symptomatic and presymptomatic plant diagnosis, for patient stratification in pharmaceutical product development and for therapeutic

20 medicament selection, for detecting pathogens and harmful substances, in particular salmonellae, prions, viruses and bacteria, in particular in foodstuffs analysis and ecological analysis.

90. The use of a method as claimed in one of claims 1-49 and/or of an analytical system as claimed in one of claims 50-88 in nonlinear optics, material research, investigation of processes at phase boundaries and surfaces of solid bodies, quality control of optical components, in particular for laser technology, for example of frequency-doubling components.